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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,466	08/07/2006	Ji Hoon Jeong	2236.0180000/JUK/SMW	4435

26111 7590 05/26/2009

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EXAMINER	
PITRAK, JENNIFER S	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
05/26/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,466	JEONG ET AL.	
	Examiner	Art Unit	
	JENNIFER PITRAK	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/17/2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *9-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Remarks

The finality of the 07/17/2008 Office Action is withdrawn in view of the Pre-Brief Conference decision of 03/19/2009. Claims 1-8 are under examination. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102 - withdrawn

The rejection of claims 1-7 under 35 U.S.C. 102(b) as being clearly anticipated by Tullis (1990, US Patent 4,904,582) is withdrawn. Applicant's arguments were persuasive.

Claim Rejections - 35 USC § 103 - withdrawn

The rejection of claim 8 under 35 U.S.C. 103(a) as being unpatentable over Raschella, *et al.* (1992, Cancer Research, v.52:4221-4226) and Tullis (1990, U.S. Patent 4,904,582) is withdrawn. Applicant's arguments were persuasive.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-7 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Jeong, et al. (2003, Bioconjugate Chemistry, v.14:473-9) (published on-line 03/05/2003).

The claims are to a conjugate for gene transfer comprising an oligonucleotide intended to be transferred into a target cell and a hydrophilic polymer (claim 1), wherein the polymer is a non-ionic polymer having a molecular weight greater than 500 daltons and wherein the oligonucleotide has a molecular weight between 1,000 and 50,000 daltons (claims 2 and 3). Claim 4 is to the conjugate of claim 1 wherein the polymer is polyethylene glycol (PEG). Claims 5-7 are to the conjugate wherein the oligonucleotide is an antisense oligonucleotide that is linked to the polymer by an acid-cleavable linkage and wherein the nucleotides are linked by phosphodiester bonds.

Jeong, et al. teach a c-myb-targeted antisense oligonucleotide covalently conjugated to PEG via an acid-cleavable phosphoramidate linkage (abstract). Therefore, Jeong, et al. clearly anticipate the instant claims.

Claim Rejections - 35 USC § 103 - new

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tullis (1990, US Patent 4,904,582, of record) and Goodchild (1990, Bioconj. Chem., v.1:165-187).

Tullis describes oligonucleotide conjugates for transport across cellular membranes for modulating gene expression (abstract). In Table 1 in column 19, Tullis discloses the "MBF 20 antisense C_2-PEG" probe that is antisense to mouse Beta-globin mRNA and comprises a 20-nucleotide phosphodiester-linked molecule conjugated to PEG (M_r = 3500). According to the website, www.newton.dep.anl.gov, a 20-nucleotide single-stranded DNA molecule has a

molecular weight of approximately 6600 daltons (330 daltons per nucleotide). Tullis teaches that the PEG group can be added to 5'- or 3'-end of the antisense oligonucleotide by various protocols (column 5 line 44 to column 6 line 8). Tullis does not teach the antisense oligonucleotide covalently linked to PEG via an acid-cleavable linker.

Goodchild teaches that conjugate groups such as PEG can be covalently linked to oligonucleotides by hydrozone formation (p.171, section *i*, "Reactions of Primary Alkylamines").

It would have been obvious to make the antisense oligonucleotide-PEG conjugate taught by Tullis with a hydrozone bond as the covalent linkage between PEG and the ODN. Tullis teaches that various protocols for linking PEG to ODNs can be used and Goodchild teaches that linkage by hydrazone bond formation is a protocol for doing so. Thus, one of skill in the art would recognize that the hydrozone bond formation is a simple substitution of one PEG-ODN linkage for another. Therefore, claims 1-7 would have been obvious to one of skill in the art at the time of the instant application.

Claims 1-8 rejected under 35 U.S.C. 103(a) as being unpatentable over Tullis and Goodchild as applied to claims 1-7 above, and further in view of Bennett, *et al.* (1994, J. Clin. Invest., v.93:820-828).

Claims 1-7 are described above. Claim 8 is to a conjugate for gene transfer comprising a *c-myb*-targeted antisense oligonucleotide covalently linked to a hydrophilic polymer.

Bennett, *et al.* teach *c-myc*-targeted antisense oligonucleotides and inhibition of *c-myc* expression with the antisense oligonucleotides (abstract; pp.822-5). The oligonucleotides were useful for reducing neointimal formation following balloon injury to rat arteries (p.825) and may

serve as useful therapeutics for prevention of angioplasty-induced pathologies (p.828). Bennett, *et al.* do not teach *c-myc* antisense oligonucleotides covalently linked to a hydrophilic polymer via an acid-cleavable linkage.

Tullis teaches oligonucleotides conjugated to PEG as described above (35 USC §102 rejection). Tullis teaches that the oligonucleotide-polymer conjugates are "more efficient in membrane transport, so as to be capable of crossing the membrane and effectively modulating a transcriptional system" (Abstract). At column 2, "Description of the Specific Embodiments", Tullis explains that "the amphiphilic nature of the product [oligonucleotide-polymer conjugates] aids in the transport of the conjugate across the cellular membrane and can provide additional advantages, such as increasing aqueous or liquid solubility of nucleic acid derivatives."

Goodchild teaches that conjugate groups such as PEG can be covalently linked to oligonucleotides by hydrozone formation (p.171, section *i*, "Reactions of Primary Alkylamines").

It would have been obvious to make a *c-myc*-targeted antisense oligonucleotide as taught by Bennett, *et al.* conjugated to PEG as taught by Tullis and linked via an acid-cleavable linker as taught by Goodchild. One would have been motivated to make the antisense conjugate because Bennett, *et al.* demonstrated that targeting *c-myc* by antisense was useful for reducing *c-myc* expression and neointimal formation following balloon injury and that such antisense may serve as a therapeutic for angioplasty-induced pathologies. One would be motivated to conjugate the antisense oligonucleotide (ODN) to PEG because Tullis taught that conjugating ODNs to polymers such as PEG provided more efficient transmembrane transport of the oligonucleotides. One would have recognized that hydrazone bond formation was one of several means of conjugating PEG to the ODN, as taught by Goodchild and described in the previous rejection.

One would have a reasonable expectation of success in making the conjugates because Tullis demonstrated successful use of such conjugates for targeting the mouse Beta-globin mRNA (see 35 USC §103 rejection above) and Goodchild teaches that hydrazone bonds have successfully been used to add conjugate groups to ODNs (pp171-2). Thus, the instant claims would have been obvious to one skilled in the art at the time of the instant application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER PITRAK whose telephone number is (571)270-3061. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Pitrak
Examiner
Art Unit 1635

/Sean R McGarry/
Primary Examiner, Art Unit 1635